

Claims

1. A combination product comprising:

5 (a) a compound of claim 1 in WO 02/44145 or a pharmaceutically-acceptable derivative thereof; and

(b) (1) a compound as defined in claim 1 of WO 01/28992 or (2) a compound of Claim 34 of WO 01/28992 or (3) Compound A or B or C or D (or pharmaceutically-acceptable salts thereof)

10 wherein each of components (a) and (b) is formulated in admixture with a pharmaceutically-acceptable adjuvant, diluent or carrier.

2. A combination product as claimed in Claim 1 which comprises a pharmaceutical

15 formulation including a compound of claim 1 in WO 02/44145 or a compound of claim 20 in WO 02/44145 or sub-set 1, 2 or 3 of the compounds of claim 20 or a pharmaceutically-acceptable derivative thereof, and (1) a compound as defined in claim 1 of WO 01/28992 or (2) a compound of Claim 34 of WO 01/28992 or (3) Compound A or B or C or D (or pharmaceutically-acceptable salts thereof) or a pharmaceutically-acceptable derivative thereof, in admixture with a pharmaceutically-acceptable adjuvant, diluent or carrier.

20 3. A combination product as claimed in Claim 1 which comprises a kit of parts comprising components:

(a) a pharmaceutical formulation including a compound of claim 1 in WO 02/44145 or a compound of claim 20 in WO 02/44145 or sub-set 1, 2 or 3 of the compounds of claim 20 or a pharmaceutically-acceptable derivative thereof, in admixture with a pharmaceutically-acceptable adjuvant, diluent or carrier; and

(b) a pharmaceutical formulation including (1) a compound as defined in claim 1 of WO 01/28992 or (2) a compound of Claim 34 of WO 01/28992 or (3) Compound A or B or C or D (or pharmaceutically-acceptable salts thereof), in admixture with a pharmaceutically-acceptable adjuvant, diluent or carrier.

which components (a) and (b) are each provided in a form that is suitable for administration in conjunction with the other.

4. A kit of parts as claimed in Claim 3, wherein components (a) and (b) are suitable for sequential, separate and/or simultaneous use in the treatment of a condition where

5. anticoagulant therapy is indicated.

5. A combination product as claimed in any one of Claims 1 to 4, which comprises Compound A or B or C or D (or pharmaceutically-acceptable salts thereof).

10 6. A combination product as claimed in any one of Claims 1 to 5 wherein the compound of WO 02/44145 is selected from:

Ph(3-Cl)(5-OCHF₂)-(R)CH(OH)C(O)-Aze-Pab;

15 Ph(3-Cl)(5-OCF₃)-(R)CH(OH)C(O)-Aze-Pab;

Ph(3-Cl)(5-OCHF₂)-(S)CH(CH₂OH)C(O)-Aze-Pab;

Ph(3-Cl)(5-OCF₃)-(S)CH(CH₂OH)C(O)-Aze-Pab;

Ph(3-OCHF₂)-(R)CH(OH)-CO-Aze-Pab;

Ph(3-OCF₃)-(R)CH(OH)-CO-Aze-Pab;

20 Ph(3-Cl)(5-OCH₂CF₃)-(R)CH(OH)C(O)-Aze-Pab;

Ph(3-Cl)(5-OCH₂CHF₂)-(R)CH(OH)C(O)-Aze-Pab;

Ph(3-Cl)(5-OCH₂F)-(R)CH(OH)C(O)-Aze-Pab;

Ph(3-Cl)(5-OCH₂CH₂F)-(R)CH(OH)C(O)-Aze-Pab;

Ph(3-Cl)(5-OCH(CH₂F)₂)-(R)CH(OH)C(O)-Aze-Pab;

25 Ph(3-F)(5-OCHF₂)-(R)CH(OH)C(O)-Aze-Pab;

Ph(3-Br)(5-OCH₂F)-(R)CH(OH)C(O)-Aze-Pab;

Ph(3-Br)(5-OCHF₂)-(R)CH(OH)C(O)-Aze-Pab;

Ph(3-Cl, 5-OCHF₂)-(R)CH(OH)C(O)-Pro-Pab;

Ph(3-Cl, 5-OCHF₂)-(R)CH(OH)C(O)-Aze-NH-CH₂-((2-amidino)-5-pyridinyl);

Ph(3-Cl, 5-OCHF₂)-(R)CH(OH)C(O)-Aze-NH-CH₂-((5-amidino)-2-pyrimidinyl);

30 Ph(3-Cl, 5-OCHF₂)-(R)CH(OH)C(O)-Aze-Pab(3-F);

Ph(3-Cl, 5-OCHF₂)-(R)CH(OH)C(O)-Aze-Pab(3-F);

Ph(3-Cl, 5-OCHF₂)-(R)CH(OH)C(O)-Aze-Pab(2,6-diF);
Ph(3-Cl, 5-OCHF₂)-(R)CH(OH)C(O)-Aze-Pab(2,5-diF).
Ph(3-Cl)(5-OCHF₂)-(R)CH(OH)C(O)-Aze-Pab(OMe);
Ph(3-Cl)(5-OCHF₂)-(R)CH(OH)C(O)-Aze-Pab(OEt);
5 Ph(3-Cl)(5-OCHF₂)-(R)CH(OH)C(O)-Aze-Pab(OnPr);
Ph(3-Cl)(5-OCHF₂)-(R)CH(OH)C(O)-Aze-Pab(OiPr);
Ph(3-Cl)(5-OCHF₂)-(R)CH(OH)C(O)-Aze-Pab(OcBu);
Ph(3-Cl)(5-OCHF₂)-(R)CH(OH)C(O)-Aze-Pab(OH);
Ph(3-Cl)(5-OCHF₂)-(R)CH(OH)C(O)-Aze-Pab(COOCPentyl);
Ph(3-Cl)(5-OCHF₂)-(R)CH(OH)C(O)-Aze-Pab(Z);
10 Ph(3-Cl)(5-OCF₃)-(R)CH(OH)C(O)-Aze-Pab(OMe);
Ph(3-Cl)(5-OCF₃)-(R)CH(OH)C(O)-Aze-Pab(OCH₂-3-(5-Me-isoxazole));
Ph(3-Cl)(5-OCF₃)-(R)CH(OH)C(O)-Aze-Pab(OCH₂-3-pyridine);
Ph(3-Cl)(5-OCF₃)-(R)CH(OH)C(O)-Aze-Pab(OiBu);
15 Ph(3-Cl)(5-OCF₃)-(R)CH(OH)C(O)-Aze-Pab(OEt);
Ph(3-Cl)(5-OCF₃)-(R)CH(OH)C(O)-Aze-Pab(Obn);
Ph(3-Cl)(5-OCF₃)-(R)CH(OH)C(O)-Aze-Pab(OcHexyl);
Ph(3-Cl)(5-OCF₃)-(R)CH(OH)C(O)-Aze-Pab(OcBu);
Ph(3-Cl)(5-OCF₃)-(R)CH(OH)C(O)-Aze-Pab(OCH₂CH₂OPh(3-CF₃));
20 Ph(3-Cl)(5-OCF₃)-(R)CH(OH)C(O)-Aze-Pab(Obn(4-Cl));
Ph(3-Cl)(5-OCF₃)-(R)CH(OH)C(O)-Aze-Pab(Obn(3-MeO));
Ph(3-Cl)(5-OCF₃)-(R)CH(OH)C(O)-Aze-Pab(Obn(2-Br));
Ph(3-Cl)(5-OCF₃)-(R)CH(OH)C(O)-Aze-Pab(Obn(4-Me));
Ph(3-Cl)(5-OCF₃)-(R)CH(OH)C(O)-Aze-Pab(O-4-heptyl);
25 Ph(3-Cl)(5-OCF₃)-(S)CH(CH₂OH)C(O)-Aze-Pab(OMe);
Ph(3-Cl)(5-OCH₂CF₃)-(R)CH(OH)C(O)-Aze-Pab(OMe);
Ph(3-Cl)(5-OCH₂CHF₂)-(R)CH(OH)C(O)-Aze-Pab(OMe);
Ph(3-Cl)(5-OCH₂CH₂F)-(R)CH(OH)C(O)-Aze-Pab(OMe);
30 Ph(3-Cl)(5-OCH(CH₂F)₂)-(R)CH(OH)C(O)-Aze-Pab(OMe);
Ph(3-F)(5-OCHF₂)-(R)CH(OH)C(O)-Aze-Pab(OMe);
Ph(3-Br)(5-OCHF₂)-(R)CH(OH)C(O)-Aze-Pab(OMe);

Ph(3-Cl, 5-OCH₂CHF₂)-(R)CH(OH)C(O)-Aze-Pab(OH);
Ph(3-Cl, 5-OCH₂CH₂F)-(R)CH(OH)C(O)-Aze-Pab(OH);
Ph(3-Cl, 5-OCHF₂)-(R)CH(OH)C(O)-Pro-Pab(OMe);
Ph(3-Cl, 5-OCHF₂)-(R)CH(OH)C(O)-Aze-NH-CH₂-((2-methoxy-amidino)-5-pyridinyl);
Ph(3-Cl, 5-OCHF₂)-(R)CH(OH)C(O)-Aze-NH-CH₂-((5-methoxy-amidino)-2-pyrimidinyl);
5 Ph(3-Cl, 5-OCHF₂)-(R)CH(OH)C(O)-Aze-NH-CH₂-((2,6-diF)(OMe); or
Ph(3-Cl, 5-OCHF₂)-(R)CH(OH)C(O)-Aze-Pab(2,6-diF)(OMe) and pharmaceutically-
acceptable derivatives thereof.

10 7. A method of making a kit of parts as defined in any one of Claims 3 to 6, which method
comprises bringing a component (a), as defined in any one of Claims 3 to 6, into
association with a component (b), as defined in any one of Claims 3 to 6, thus rendering
the two components suitable for administration in conjunction with each other.

15 8. A kit of parts comprising:
(I) one of components (a) and (b) as defined in any one of Claims 3 to 6; together with
(II) instructions to use that component in conjunction with the other of the two
components.

20 9. A method of treatment arrhythmia, which comprises administration of a combination
product as defined in any one of Claims 1 to 8 to a patient suffering from, or susceptible to,
such a condition.

25 10. The use of a combination product as defined in any one of Claims 1 to 8 for the
manufacture of a medicament for the treatment or prophylaxis of a condition where
anticoagulant therapy is indicated.

11. The use of a compound of claim 1 in WO 02/44145 or a compound of claim 20 in WO
02/44145 (or derivative thereof) or a pharmaceutically-acceptable derivative thereof and
30 (1) a compound as defined in claim 1 of WO 01/28992 or (2) a compound of Claim 34 of

WO 01/28992 or (3) Compound A or B or C or D (or pharmaceutically-acceptable salts thereof) for the manufacture of a medicament for the treatment or prophylaxis of a condition where anticoagulant therapy is indicated.